ZVONIMIR MAJIĆ, B.Eng.
E-mail: zvonimir.majic@austrian.com
Austrian Airlines
Pleso bb, HR-10150 Zagreb, Republic of Croatia
IRENA JUKIĆ, MD
E-mail: irena.jukic@hztm.hr
Croatian Institute of Transfusion Medicine
Petrova 3, HR-10000 Zagreb, Republic of Croatia
STANISLAV PAVLIN, Ph.D.
E-mail: stanislav.pavlin@fpz.hr
University of Zagreb,
Faculty of Transport and Traffic Sciences
Vukelićeva 4, HR-10000 Zagreb, Republic of Croatia

Distribution Logistics
Review
Accepted: June 16, 2009
Approved: Oct. 22, 2009

AIR TRANSPORT AND LOGISTICS IN PANDEMIC OUTBREAK OF INFLUENZA A (H1N1) VIRUS

ABSTRACT

In April 2009, the WHO, (World Health Organization) evaluated the available data on the swine influenza A (H1N1), confirmed the outbreak and declared decision on raising the pandemic phase from five to six. IATA, (International Air Transport Association) invited the airlines to support WHO's reference laboratories around the world in handling specimens should the outbreak expand further. The specimens shall be transported according to the regulations stipulated for acceptance and transportation of dangerous goods by air. The paper analyses the current infrastructural situation at the airports in Croatia, predispositions related to the trained staff and coordination procedures with the relevant institutions. The implementation of activities complying with the international regulations are suggested in order to conduct measures fighting the pandemic in Croatia.

KEY WORDS

pandemic outbreak, regulation, recommendation, specimen, responsibilities, transportation and logistic for biological substances

1. INTRODUCTION

Influenza (the flu) is an acute infectious disease of the respiratory system caused by one of the influenza viruses. It occurs in the form of larger or smaller epidemics and pandemics. Clinically, along with high temperature during two to five days, the most common symptoms are general tiredness and weakness, respiratory symptoms are usually not strong, but the tendency to complications is especially present in older persons and persons suffering from other diseases. The influenza viral particles are transmitted by coughs or sneezes. They are typically transmitted by air, via large drops of nasal secretions, in close contact within closed areas. The infected person emits while talking, sneezing, coughing small droplets into the environment, which may contain viral particles. These droplets may then reach another person and enter their organism through the mucous membrane of the nose and/or mouth. They may also be transmitted in direct contact with the infected person and the infected items.

Influenza is caused by one of the three influenza viruses: *Influenzavirus A*, *Influenzavirus B* and *Influenzavirus C* from the family Orthomyxoviridae. On their surface they have two antigens – proteins hemagglutinin (H) and neuraminidase (N), 10-12nm long. They allow numerous variations i. e. changes in the antigen structure and they occur almost every year. This is how new subtypes of the influenza viruses are formed. New influenza viruses are constantly produced due to the mutations and reassortment of gens. Mutations can cause small changes in the hemagglutinin and neuramidase antigens on the virus surface. This is called antigenic drift, responsible for the creation of new host species. When the new virus variant achieves greater capability and becomes dominant it "flies through" the human population – often sporadic cases and limited epidemics.

On the other hand, by genetic reassortment the viruses may acquire new antigens, e. g. recombination of gens between animal and human species. This is antigenic shift. If a human influenza virus occurs with new, unknown antigens, everybody will be susceptible. The new flu will expand without control, causing epidemics/pandemics.

Sixteen HA subtypes and nine NA subtypes have been known. Various combinations of HA and NA

proteins are possible. Only some influenza subtypes are in general circulation among people (H1N1, H1N2, H3N2). Other subtypes have been found in other animal species. E. g. H7N7 and H3N8 viruses cause disease in horses, and H3N8 also in dogs. It is precisely these changes that make it impossible to develop permanent immunity to influenza; if antibodies are developed one year for a certain type of the flu virus, they will probably provide no protection against a new type of flue in another year. Three types of influenzaviruses A, B and C, apart from the antigenic structure differ also according to their epidemic potential. Influenzavirus A has the highest epidemic potential and it is the "most unpredictable" one since its surface antigens change most frequently. The latter virus occurs as the cause of all the pandemics and larger epidemics. Virus B has the lowest epidemic potential, i. e. antigenic variations occur less frequently, whereas these changes occur very rarely in case of virus C. Also, the influenzaviruses differ regarding the severity of disease they cause. Influenzavirus A causes more severe disease, influenzavirus B less severe, and influenzavirus C very mild disease which may even pass without being recognized.

In the revision of the description of the pandemics phases in 2009, WHO retained the six phases, incorporating new recommendations and approaches to the already existing national recommendations and plans. The first

The first three phases define the procedures and actions regarding the preparedness to act in case of the onset of a pandemic, whereas phases four and six call for concrete measures to be undertaken in implementing the plan for the defence against the pandemic. Two phases represented in Figure 1 after the fifth, i. e. sixth phase refer to the post-pandemic handling and evaluation of the situation.

The phases differ also regarding the potential of the influenza virus to cause infection and to "skip" to other biological species, i. e. to cause epidemics and/or pandemics. In nature, the influenzavirus circulates continuously among animals, especially birds. Although such a virus can theoretically develop into a pandemic virus, in **Phase 1** no such virus has been described as the cause of infections in humans. In **Phase 2** the animal influenzavirus circulates among domestic and wild animals, causes infections in humans and there is potential threat of a pandemics. In **Phase 3** animal or human-animal influenza reassorted virus causes random cases or infections in small human communities, but there is no transmission from human to human to such an extent to have an outbreak of infection within a wider community. The limitation of the transmission from human to human may appear e. g. in closed communities where there is contact between the infected person and a member of the closest family. The limited transmissions within closed communities do not mean that the virus will pass to the higher phase and cause a pandemics in the wider community. **Phase 4** is characterized by the proven transmission of the animal influenzavirus from human to human or the proof of an a human-animal influenza reassorted virus within the community. If such a case is suspected or confirmed, every state should immediately consult the World Health Organization in order to make decisions on further activities. Phase 4 shows significant increase in the risk of pandemics, but this does not necessarily mean pandemics itself.

Phase 5 is characterised by the spreading of the viral infection from human to human in at least two

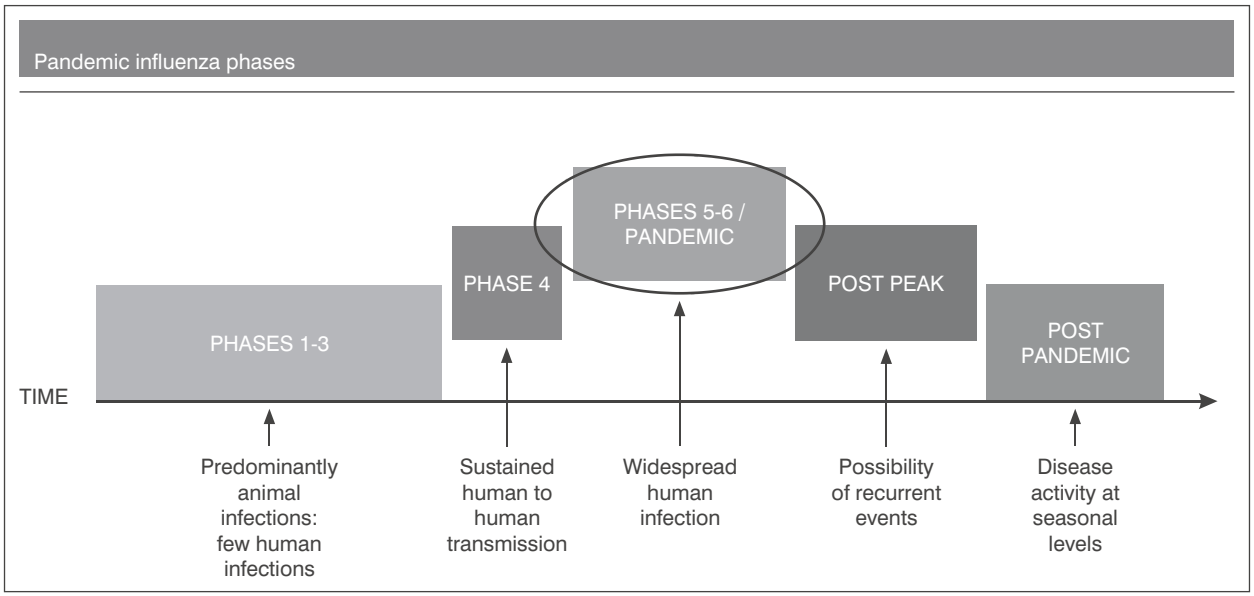

Figure 1 – Phases of preparedness and response to outbreak of pandemic, June 2009

Source: WHO; Weekly epidemiological record, No. 25; 19 June 2009

Table 1 – Characteristics of three pandemics in the 20th century

Pandemic (date and common name	Area of emergence	Influenza A virus subtype	Estimated reproductive numbar	Estimated case fatality rate	Estimated attributable excess mortality worldwide	Age groups most affected (simulated attack rates)	GDP loss (percentage change)[6 7]
1918-1919 "Spanish Flu"	Unclear	H1N1	1.5-.8	2-3%	20-50 million	Young adults	-16.9 to 2.4
1957-1958 "Asian Flu"	Southern China	H2N2	1.5	<0.2%	1-4 million	Children	-3.5 to 0.4
1968-1969	Southern China	H3N2	1.3-1.6	<0.2%	1-4 million	All age groups	-0.4 to (-1.5)

Source: WHO; Pandemic Influenza Preparedness and Response, Geneva, Switzerland, April 2009.

countries within one region. Proclaiming phase 5 means strong warning of a pandemic threat, and invites prompt action regarding organization, communication, and implementation of the planned measures to mitigate the consequences. **Phase 6** of the pandemics is characterised by the spreading of infection in at least one country of another region. When this phase is proclaimed it means that the global pandemics is present. Adequate control of its spreading can prevent or at lease mitigate the occurrence of a new wave.

According to the definitions of contagious diseases defined by the Croatian National Institute of Public Health, and adopted on the basis of the European Commission document[1], the onset of influenza has been defined through three segments:

- clinical description or clinical picture compatible with the flu and characterized by the sudden onset of the disease, cough, fever, muscle ache, headache, and increased temperature (over 38°C);
- laboratory criterion for the diagnosis has been defined by laboratory certificate in one of the following three ways:
  - influenza antigen finding or RNA specific for influenza finding;
  - isolation of the influenza virus;
  - evidence of response specific for serum anti-body to influenza A or B.
- Classification of the influenza virus case occurrence is contained in three basic categories:
  - Possible: not applied;
  - Probable: clinically compatible case with epidemiological relation;
  - Confirmed: laboratory confirmed clinical case.

The central institution for the control and monitoring of epidemiological diseases in the Republic of Croatia is the epidemiology unit of the Croatian National Institute of Public Health. Its function is centralized monitoring and control of the disease, and from this aspect it has the character of a national centre for disease control. The unit acts as part of the authorities contained in the Act on Health Care and the Act on the Protection of the Population against Communicable Diseases. The scope of the unit's activities covers also the procedures and tasks of monitoring and analysis of the epidemiological situation on the territory of Croatia, proposal of anti-epidemiological measures and supervision of their implementation, coordination, and implementation of the cooperation between the county institutes for public health, and cooperation with the department for emergency situations of the Ministry of Health. The scope of epidemiological control contains the activities and procedures towards persons suffering of contagious disease as well as towards persons that had contact with the diseased person. The supervision and epidemiological control will be carried out also over persons who arrived from the area in which the influenza has been evidenced.

Under the conditions of global pandemic outbreak, the role of reference laboratories of the World Health Organization in timely confirmation of the virus presence within a certain geographical area is of crucial importance in area localization and application of adequate measures fighting the virus. Taking samples from persons who are suspected to have the virus in order to determine the presence of the virus as well as sending of specimens to reference laboratory centres is very significant for further timely undertaking of protective measures. Because of the high speed at which the pandemic spreads, it is to be expected that the specimens of the potentially diseased persons will be exchanged using air transport. Short time period after taking the specimens until receiving the reference finding is of crucial significance in the pandemic control and further undertaking of adequate measures.

2. AIR TRANSPORT AND PANDEMIC, CAUSE-EFFECT RELATION

One of the most frequent modes of fast epidemic spreading and occurrence of pandemic is precisely air

transport. Because of emphasized capability of overcoming large distances within a short period of time, air transport represents potentially significant threat to the control and localization of the virus within a certain area. Often the carriers of epidemiological diseases in the first phases of investigation are sought precisely in passengers who have arrived from the potentially infected areas by aircraft.

The aircraft air circulation system also represents potentially favourable environment for the spreading of airborne viruses. Airborne diseases as well as indications and risks related to their onset are defined in the WHO document entitled "International Travel and Health 2009". This document defines airborne transmission of diseases with the following definition: "*Airborne transmission occurs when droplet nuclei (evaporated droplets) <5 micron in size are disseminated in the air. These droplet nuclei can remain suspended in the air for some time. Droplet nuclei are the residuals of droplets and when suspended in the air, they dry and produce particles ranging in size from 1–5 microns*." The virus droplets are transmitted via nose or mouth mucous membrane provided there is close contact with the infected person. Virus droplets are absorbed by breath intake while coughing or sneezing of the infected person.

Tourist trips are related to certain geographic regions during a certain season which may contribute to fast spreading of the virus from a certain area. At the same time, virus transmission from one geographic and climatic area to another can have influence on the virus image in the new environment. The prevention and protection against influenzas can thus be made additionally difficult by the occurrence of new subtypes of viruses from another geographic environment. The initial measures to control the spread of the epidemic i. e. pandemic can be recognized precisely at airports in a whole series of the for-the-given-moment adequate procedures. Surveying and registration of passengers arriving from potentially contagious areas, establishing of direct testing at airports all the way to accommodation of passengers in quarantines.

Another aspect of the relation between air transport and pandemic spread can be recognized in the need to transport specimens taken from the diseased or potentially infected persons in order to determine the presence of a virus. In such circumstances the character of air transport and its ability to overcome huge distances within a short period of time has almost no alternative in practice. Here, attention should be directed to the basic characteristics of the transport entity as well as the valid national and international provisions regulated for the transport of this type of entity.

Finally, air transport represents the key transport mode for the pandemic preventive vaccines. Large quantities of vaccines transported within the shortest time possible are the precondition to fast and efficient response to a pandemic. Attention should be also directed to the character of the vaccine as transport entity recognizing strict national and international regulations defined in documents on good production and distribution practice.

3. CHARACTER OF BIOLOGICAL PHARMACEUTICAL PRODUCTS AS TRANSPORT ENTITIES

Transport entities previously known as clinical specimens, diagnostic specimens or blood samples and preparations, are regulated and defined by coming into force of the new regulation published in the IATA Dangerous Goods Regulations, 48th Edition, of 1 January 2007. All the mentioned categories are combined under the title of biological substances with the latter being even possibly restrictive compared to the valid regulations related to transport. Apart from the mentioned classification, the classification of the biological substances was also published by ICAO (International Civil Aviation Organization), according to the key presented in Figure 2.

Biological samples are materials or pharmaceutical products of human or animal origin. Unlike chemical pharmaceutical products which include drugs and medical preparations for human use produced by chemical processes, biologically produced pharmaceuticals are characterized precisely by the biological environment of the production. In the ICAO document *Technical instructions for the safe transport of dangerous goods by air*, 2007-2008 Edition, biological substances are defined as specimens of human or animal origin collected by secretion or extraction directly from the patient, human or animal, in the form of blood or its components, physiological secretion, tissue, parts of body or organs being transported for purposes such as diagnosis, research activities, or the needs of medical treatment and prevention of various diseases.

Isolated from the biological production environment, the specimens are time and temperature sensitive. This is precisely the reason why they represent a complex and demanding transport entity. Regarding time, the biological products are characterized by disposability and non-reproducibility of the original form of production, and a short lifecycle. Therefore, they are sensitive also to exposure to temperature oscillations different from the production ones, at the same time not limited only to the latter.

Temperature distribution regimes depend on the type of biological products as transport entities. The biological substances, for instance, can be transported at tempera-

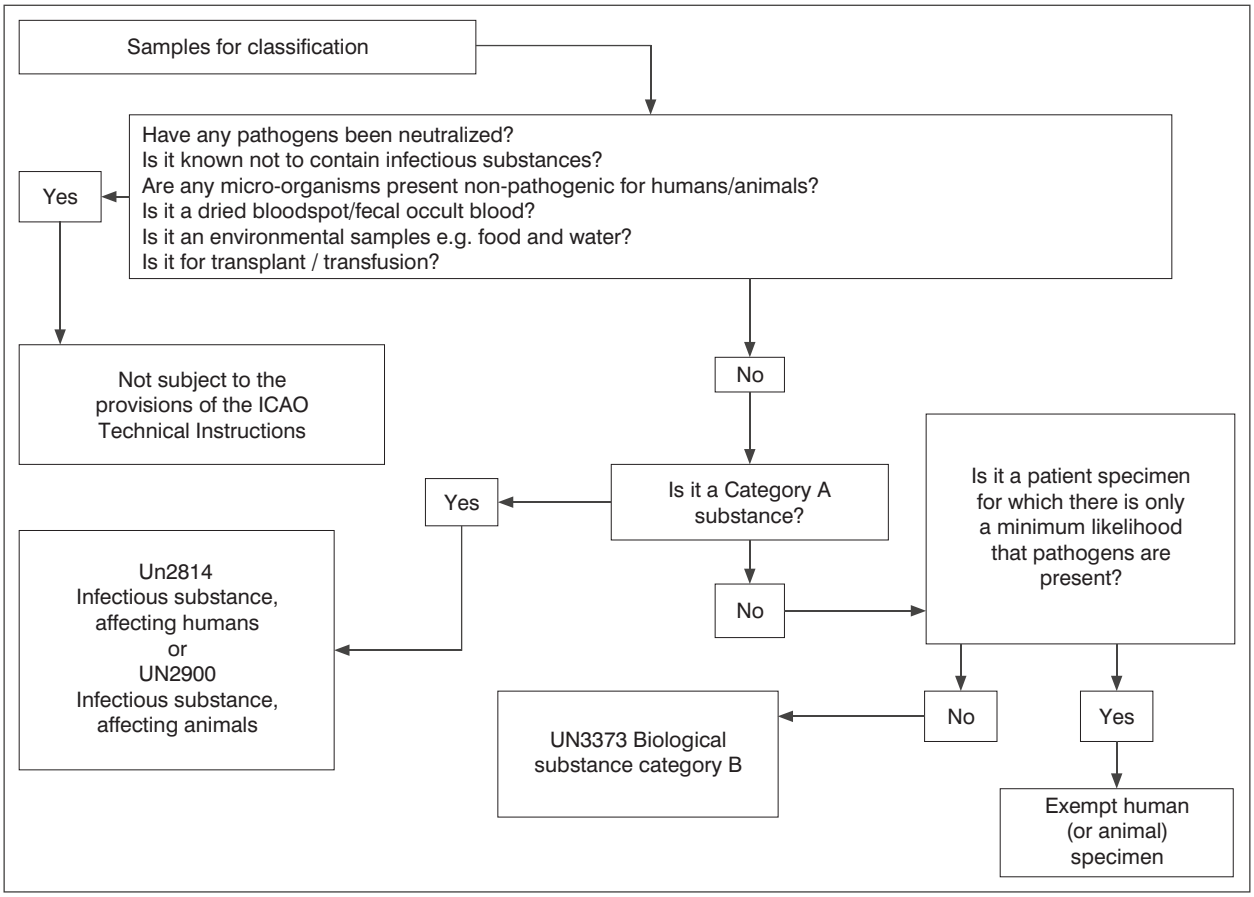

Figure 2 – Classification of biological substances

Source: ICAO document; Technical instruction for the Safe Transport of Dangerous Goods by Air, Annex 2, 2005-2006

tures from deepfreeze conditions at -70°C, to ambient temperature ranging from +15°C to +25°C. Vaccine as biological pharmaceutical product is distributed mainly in the range of positive temperature values with possible temperature excursions even up to +30°C without, conditionally speaking, influence on the vaccine quality. Should vaccine be exposed at the same time to temperature of 0°C or lower, its quality is questionable and this may result in the recall of the vaccine from the market. The conditions of distributing biological substances or vaccines as well as temperature ranges to which a product can be exposed in the distribution environment are defined by the producer respecting the findings of stability studies.

According to data from the year 2007 Zagreb Airport occupied a significant place in the traffic of biological substances in the Republic of Croatia, with a total of 1052 biological substances handled in export. The calculation based on 12 months a year and the average of 21 workdays in a month, indicates the average of approximately four shipments per day. The latter calculation can be presented in a more precise form if exact dates of every single shipment and the seasonal characteristic present in this case as well are taken into consideration. The figure of four biological substances a day shipped from Zagreb Airport during 2007, when there was no officially proclaimed threat of pandemic in the environment, may indicate the presence of a significant degree of frequency in the transport of biological substances in Croatia. Here the consideration may include also the character of the shipped biological substances, in order to obtain a more concrete picture and profile of shipments. Based on the frequency considerations regarding single shippers at certain shipment frequency it may be concluded that the shipments were mostly the result of research carried out regarding implementation of a preparation on a target group of patients. More precise data on the number of specimens within a defined period of time cannot be presented due to the confidentiality of data related to the sponsored studies. It remains to be concluded that in regular circumstances, when there is no potential threat of pandemic outbreak of a certain virus, the majority of treated biological substances may be assigned to clinical studies.

4. TECHNOLOGY OF HANDLING BIOLOGICAL PHARMACEUTICALS

The responsibilities of each single mentality within the technological process of transporting bio-

logical substances have been defined by IATA Dangerous Goods Regulations speaking about biological substances, or by the Perishable Cargo Regulations considering vaccines. By considering the distributive environment one may recognise several phases of the technological process of transportation. The preparation phases are characterized by procedures within the area of the responsibility of the shipper, and refer to the declaration of entities, packing, implementation and recognition of all the valid national and international regulatory liabilities in the area of distribution, and issuing of the stipulated documentation.

The acceptance phase of distribution in shipping of biological pharmaceutical products in air transport is characterized by the activities and procedures related to handling terminals (airports) and carriers, i. e. contracted legal subjects authorized to provide cargo handling services. The procedures and activities included in this phase can be recognized combined into two basic ones. Physical and documentary acceptance carrying out the supervision activities based on the control lists designed in order to check and confirm application of all the valid regulatory issues defined for the shipment of this type of transport entities. The processing of a transport entity in order to determine and document the compliance with the valid provisions regulated for the respective entity, represents the key step within the technological phase since the latter is related to the very safety of air transport. The control of the physically present entity and the accompanying documents using the stipulated and by the carrier designed control list, has the purpose of recognizing possible failures that may have occurred during the preparation phase of entity processing, and can claim through documents the preparedness of the transport entity to be forwarded to the next phase. The minimum of conditions contained in the control list are stipulated by IATA, but the carriers may be more restrictive regarding the handling conditions. The supervision activities with the application of the control list are performed by the authorized employees qualified and licensed by IATA authorized training centres, companies or legal persons. The qualification and license to perform dangerous cargo handling procedures mean completed training course and passed category 6 exam according to IATA category classification relating to dangerous goods handling. The supervision activities based on adequate control list are carried out by the carrier agents, on whose flights the transport task is to be realized. This role may be taken over also by the authorized employees of the handling terminals or third parties provided they have the required qualifications so that there is contractually regulated relation to perform the activities included in this scope.

The next phase in the technological process can be unified under the common title dispatch activities. The latter phase, as well as the previous one, is characterized by the interaction between the handling terminal and the carrier, and it refers, in the first place to the application of the valid regulations related to the technology of dispatch, as well as possible specific characteristics related to this type of dispatch and individual carriers. In the first place, one may recognize here the restrictions a carrier may have regarding dispatch of this type of entity. The restrictions may be technical (aircraft type planned for individual transport segments) or of technological character (regulated obligation of fixing the transport entity within the aircraft cargo compartment).

The last phase of the distributive process which refers to the realization of the transport task is the transport of the entity under the conditions defined and required by the shipper. The biologically produced pharmaceuticals are characterized by their time and temperature sensitivity. This is the reason for strict national and international regulations in the area of distribution as the precondition of preserving the original quality of the products until they reach the end user.

The international regulations in the distribution of temperature sensitive and restrictive pharmaceuticals clearly emphasises the need to maintain the given conditions during the distributive process. The WHO document "*Technical Report Series", No. 917, Annex 2, "Good trade and distribution practices for pharmaceutical starting materials"*, in the Section Distribution and Transport defines the expectations of the regulatory bodies in the area of transport. The transport of clinical materials shall be organized so that it shall guarantee compliance with the given conditions. The transport process shall not affect the quality of the transport entity [3].

The European Medicines Agency, in the document *Guidelines on Good Distribution Practice of Medicinal Products for Human Use 94/C 63/03, (these guidelines have been prepared in accordance with Article 10 of Council Directive 92/25/EEC of 31 March 1992 on the wholesale distribution of medicinal products for human use*), defines precisely the transport conditions for temperature sensitive and restrictive pharmaceutical products. Medicinal products as transport entities shall be protected during transport from negative impacts of temperature, light, moisture or other harmful influences [4].

Apart from the mentioned one, the European regulation contains also documents closely related to the distribution of biological substances. Directive 2005/28/EC defines the conditions of product registration and import of clinical specimens and the 2002/98/EC Directive of quality and safety standards for the collection, testing, processing, storage and distribution of human blood and blood components. The

2004/23/EC Directive defines the standards of quality and safety in collecting, testing, processing, storage and distribution of human tissues and cells.

The United States Pharmacopeia (USP), in the document: "*General Chapter 1079 Good Storage and Shipping Practice*" emphasises the temperature regime management in the distribution environment as the crucial element of the original product quality assurance: the mentalities within the technological process of distribution shall insure storage and transport conditions with the objective of protecting the transport entity under the conditions defined by the manufacturer [5].

The regulations in the Republic of Croatia are defined in the 2008 Act on Medicinal Products which in the section of general provisions emphasises the liabilities of the distribution chain participants not excluding any of the mentalities within the technological process of distribution [6].

5. DOCUMENT FOR COORDINATION OF TRANSPORT ACTIVITIES AND EPIDEMIOLOGICAL PROTECTION SERVICE

The Act on Dangerous Goods Transport from July 2007, Article 28, Items 2 and 3 define the obligation to appoint an expert counsellor as well as the obligation to keep register of the employees qualified and licensed to perform the activities of expert counsellor in the area of handling dangerous cargo in air traffic. This Act does not plan for the register of qualified and licensed employees employed by the foreign carriers, nor the register of employees qualified and licensed either in Croatia or abroad, for handling perishable cargo in air traffic. It may therefore be concluded that there is no central register of the qualified and licensed employees for the handling of dangerous or perishable cargo in air traffic in the Republic of Croatia.

The central register of the available number of licensed employees may represent an advantage in the organization and implementation of the protection measures in case of a pandemic in a certain region. Apart from this data, the data on the available refrigeration capacities for individual handling terminals may also be assessed as significant. For instance, the distribution of vaccines by aircraft to Split may be assessed as a demanding task since the refrigeration capacities of the handling terminal are limited. In such circumstances the alternative solutions result from the need to improvise which may represent a risk. Table 2 shows data on the capacities of refrigeration chambers at cargo terminals of three busiest airports in Croatia, obtained by carrying out a survey among the handling services managers during March 2009.

Table 2 – Data on available refrigeration capacities of chambers at three busiest airports in Croatia[2]

Airport	Chamber cold: +2°C to +8°C	Chamber deep freeze: -20°C
Split	YES / 6m^2	YES / 1m^2
Dubrovnik	NO / alternative: smaller fridge for household use	NO
Zagreb	YES / 1 x 30m^2 and 1 x 25m^2	YES / 16m^2

Source: Questionnaires filled in by managers of the authorized services

Information on temperature profiles of cargo holds of individual aircraft types are also subject to limited knowledge. In Croatia up to now no analysis has been carried out nor any determining of temperature profiles of the aircraft cargo holds of the national flag carrier. Similarly, no research has been done nor any determining of the temperature profiles of the handling terminals. Based on these facts it may be concluded that there is poor knowledge about the environment within which the temperature sensitive entities are transported.

The epidemiological unit of the Croatian National Institute of Public Health, as part of its activities, organizes and implements activities in the area of control and prevention, as well as analysis and tracking of epidemiological occurrences on the territory of the Republic of Croatia. Among other things, new vaccines are being tested and the distribution is coordinated and supervised. Based on the invitation of the World Health Organization to air carriers to provide capacities for the transport of both clinical specimens as well as vaccines, a discussion may be started about the organization and preparedness of the air transport system in Croatia to the occurrence and development of a greater volume of transporting time and temperature sensitive transportation entities. Table 2 indicates the limited available capacities for the acceptance of temperature sensitive shipments at airport terminals in Croatia.

The coordination of traffic with the activities of the epidemiological unit could mean the founding and operation of a body responsible for the registering and monitoring of the available capacities in the infrastructure, transport means and trained and licensed staff. Such a body could work as part of the scope of activities of the Civil Aviation Agency. The tasks of the coordination body for emergencies would include:

- Analysis of the condition and keeping the register of the available infrastructure for the handling of temperature sensitive shipments and dangerous cargo.
- Analysis of the condition and keeping the register of the qualified and licensed logistic operators to

perform activities in the area of handling temperature sensitive shipments and dangerous cargo.
- Analysis of the condition and keeping the register of the qualification and licenses of the staff in handling temperature sensitive shipments and dangerous cargo.
- Supervision of the implementation of the national and international regulations in the area of handling temperature sensitive shipments and dangerous cargo.
- Implementation of control over technological processes and documentation stipulated for the handling of temperature sensitive shipments and dangerous cargo.
- Analysis of the condition of infrastructure at airports in Croatia regarding the need to organize quarantine.
- Making of the regulations regarding procedures in emergency cases in air transport in case of pandemic outbreak.
- Coordination of activities with the epidemiological unit of the Croatian National Institute of Public Health.

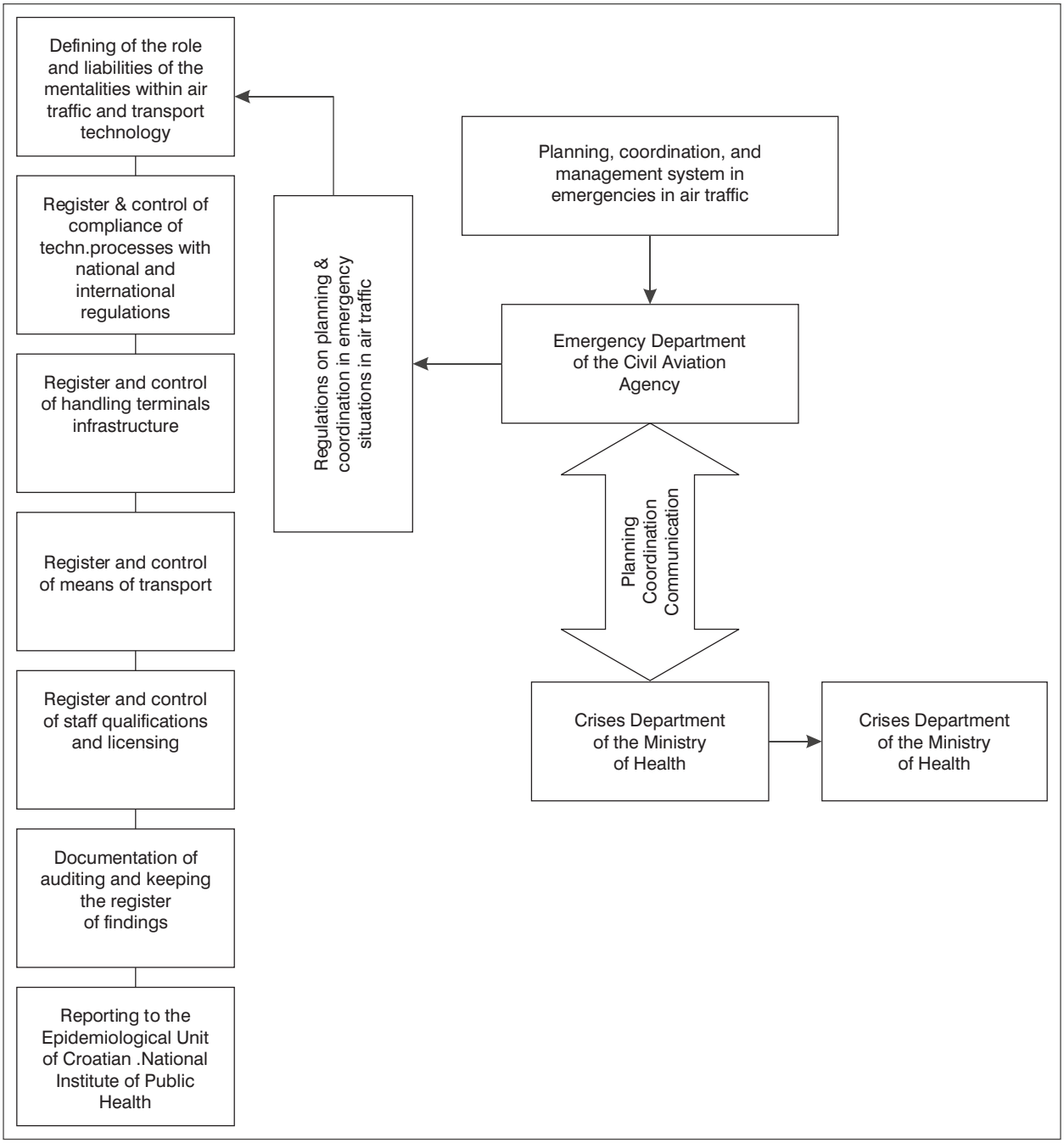

Figure 3 – Scope of activities of a possible coordination body in case of emergencies, of the Civil Aviation Agency

Source: Author

– Writing of reports on the performed supervision in accordance with the Regulations on Procedures in Emergencies in Air Traffic in case of pandemic outbreak.

Supervision belongs to the group of basic activities of the Civil Aviation Agency. The expansion of the supervision to the area of preparedness in case of pandemic outbreak as well as reporting to the Epidemiological unit can represent a valuable contribution to the organization and implementation of the measures for fighting the pandemic. Knowing the circumstances within the distributive environment for temperature sensitive shipments and shipments of dangerous cargo, as well as total passenger and cargo flows, various scenarios of emergencies may be forecast, thus actively contributing to finding good solutions.

The coordination and management of emergencies in air traffic can be included into the scope of activities of the Civil Aviation Agency with the recommendation of producing a detailed Regulations on the supervision of the implementation of adequate national and international regulations and recommendations relating to air traffic under the conditions of a pandemic outbreak.

6. CONCLUSION

The handling and transport of biological substances and vaccines is a complex technological process. The temperature oscillations, vibrations, pressure changes, exposure to light, are all part of regular occurrences in the distributive environment of air traffic. Temperature oscillations are a phenomenon which is present not only in the environment of the production, storage or manipulative infrastructure, but also in the transport means during the realization of the transport task. International regulatory bodies stipulate minimal conditions in the distribution of temperature sensitive pharmaceuticals. Companies specialized for the definition and performance of technological processes of transporting temperature sensitive and perishable cargo define the recommendations in the preparation, organization, implementation and document validation of the technological processes. Each of the mentalities within the distributive chain shall provide and carry out the stipulated standards in the distributive environment.

The biggest threat to controlled technological process of transporting temperature sensitive or dangerous cargo is the human factor. The goal of the elaborated quality control system in the defined operations of the distribution of these entities is to forecast the weak points of the system and to eliminate them. In the circumstances of increased flow of this category of transport entities it is possible to forecast also an increased occurrence of irregularities, especially in case of a lack of a developed operative plan of flow control within individual segments of the distributive environment. Formation of a body within the Civil Aviation Agency with the task of preparing and documenting the procedures in case of emergencies can contribute to greater efficiency of the total preparations for fighting against pandemic. In regular circumstances, the analysis of the total capacities and systemic monitoring of this segment of air traffic may also be a contribution to regular activities of the agency.

Air traffic on the Croatian market has no analytic document for assessing the preparedness and adjustment to the conditions of pandemic outbreak. The recommendations for the adjustment of cargo traffic system stipulated by the World Health Organization are not being implemented. The technological solutions for this type of transport entities at cargo handling terminals are not in compliance with the international regulations and recommendations. The information technology system as support to the distributive environment in cargo traffic is obsolete or inexistent. In such circumstances it may be concluded that the system is characterized by a number of potentially risky points, and as such can represent an aggravating circumstance in the organization and implementation of the measures to fight the pandemic.

ZVONIMIR MAJIĆ, dipl. ing.
E-mail: zvonimir.majic@austrian.com
Austrian Airlines
Pleso bb, 10150 Zagreb, Republika Hrvatska
IRENA JUKIĆ, dr. med.
E-mail: irena.jukic@hztm.hr
Hrvatski zavod za transfuzijsku medicinu
Petrova 3, 10000 Zagreb, Republic of Croatia
STANISLAV PAVLIN, Ph.D.
E-mail: stanislav.pavlin@fpz.hr
Sveučilište u Zagrebu, Fakultet prometnih znanosti
Vukelićeva 4, 10000 Zagreb, Republika Hrvatska

SAŽETAK

ZRAČNI PRIJEVOZ I LOGISTIKA U PANDEMIJI VIRUSA A(H1N1)

U travnju 2009. Svjetska zdravstvena organizacija ocjenjuje raspoložive podatke o virusu svinjske gripe A(H1N1), potvrđuje njegovo širenje i objavljuje odluku o podizanju faze pandemije influence sa pete na šestu. Međunarodna udruga zrakoplovnih prijevoznika upućuje poziv zračnim prijevoznicima na pružanje podrške referentnim laboratorijima Svjetske zdravstvene organizacije u prihvatu i otpremi, te zračnom prijevozu bioloških uzoraka u slučaju daljnjeg širenja pandemije. Zračni prijevoz bioloških uzoraka odvijati će se prema uvjetima definiranim za prihvat i otpremu opasnih tereta. U radu je analizirana situacija u Republici Hrvatskoj i ustanovljeno je da ne postoje infrastrukturne pretpostavke za prihvat i otpremu takvih pošiljaka u svim zračnim lukama, licencirano osoblje, koordinacija sa nadležnim javnim zdravstvenim institucijama,

te se predlažu aktivnosti kako bi se Republika Hrvatska pripremila, u skladu sa međunarodnim propisima, za provedbu mjera za obranu od pandemije.

KLJUČNE RIJEČI

izbijanje pandemije, regulativa, preporuke, biološki uzorci, područja odgovornosti, prijevoz i logistika za biološke uzorke

REFERENCE

1. Commission Decision of 19th March 2002 laying down case definitions for reporting communicable diseases to the Community network under Decision No 2119/98/EC of the European Parliament and the Council
2. Data on available refrigeration chamber capacities of three busiest airports in Croatia were collected by surveying the managers of the cargo sector of the presented airports.
3. WHO document; Technical Report Series, No. 917, Annex 2, Good trade and distribution practices for pharmaceutical starting materials.
4. EMEA document; Guidelines on Good Distribution Practice of Medicinal Products for Human Use 94/C 63/03, these guidelines have been prepared in accordance with Article 10 of Council Directive 92/25/EEC of 31 March 1992 on the wholesale distribution of medicinal products for human use.
5. USP document; General Chapter 1079 Good Storage and Shipping Practice
6. Republic of Croatia, Croatian Parliament, Act on Medicinal Products

LITERATURE

[1] World Health Organization: Global Influenza Programme, "*Pandemic Influenza Preparedness and Response*", Geneva, Switzerland, April 2009

[2] World Health Organization: Epidemic Alert & Response, "*WHO check list for influenza pandemic preparedness planning*", Geneva, Switzerland, April 2005

[3] World Health Organization: "*International Travel and Health 2009*", Situation as on 1 January 2009, Geneva, Switzerland, 2009

[4] World Health Organization: "*Collecting, preserving and shipping specimens for the diagnosis of avian influenza A(H5N1) virus infection*", Guide for field operations, Geneva, Switzerland, October 2006

[5] World Health Organization: "*Interim WHO guidance for the surveillance of human infection with swine influenza A(H1N1) virus*", Geneva, Switzerland, April 2009

[6] World Health Organization: "*International Health Regulations* (2005)", Second edition, Geneva, Switzerland, 2008

[7] International Civil Aviation Organization, Technical instruction for the Safe Transport of Dangerous Goods by Air, Annex 2, 2005-2006, Montreal, Canada

[8] **Majić Z., Pavlin S., Drljača M.**: "*Significant elements of the technological process of transporting biological substances*", 16th International Symposium on Electronics in Traffic, ITS- A condition for sustainable development and prosperity of a modern and safe transport, ISEP 2008, Electrotechnical Association of Slovenia, Ljubljana, 09th-10th October 2008., Proceedings, General, G15.

[9] International Air Transportation Association, Dangerous Goods Regulations 50th edition, Geneva, Switzerland, January 2009

[10] World Health Organization; "*Good trade and distribution practices for pharmaceutical starting materials*", WHO Technical Report Series No. 917, Annex 2, 2003

[11] The European Parliament and the European Union Council; "*Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001, on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use*".

[12] United States Pharmacopeia; General Information Chapter 1079, "*Good Storage and Sipping Practices*", Supplement 2, August 2005

[13] **Milstien J.**: "*Learning from the WHO Updated Guidelines for Storage and Monitoring of Temperature Sensitive Vaccines around the Globe*", Pharma IQ's 7th annual Cool Chain Europe Conference, Brussels, Belgium, January 2008

[14] **Taylor J., Holloway I.**: "*Transportation of Biological Products: European regulations and Guidance*", American Pharmaceutical Outsourcing, May 2007

[15] Republic of Croatia, Ministry of Health and Social Welfare; "*Act on Blood and Blood Preparations*", Zagreb, June 2006

[16] Republic of Croatia, Croatian Parliament; "*Act on Drugs*", Zagreb, June 2007

[17] Republic of Croatia, Ministry of Health and Social Welfare; "*Regulations on Clinical Testing and Good Clinical Practice*", November 2007

[18] **Majić Z., Pavlin S.**: "*Temperature profiles for carriage of perishable shipments in air transport*", 16th International Symposium on Electronics in Traffic, ITS- A condition for sustainable development and prosperity of a modern and safe transport, ISEP 2008, Electrotechnical Association of Slovenia, Ljubljana, 09th-10th October 2008., Proceedings, General, G15.

[19] **Majić Z., Pavlin S.**: "*Problematika tehnološkog procesa transporta određenih kategorija lako pokvarljivih pošiljaka*", International Scientific Symposium Development of Transport, Intelligent Transport Systems and Logistics, ZIRP 08, Faculty of Transport and Traffic Sciences, University of Zagreb, Rovinj 16-18 April 2008, e-Proceedings, Paper No. 19

[20] **Gjenero-Morgan I., Aleraj B., Kaić B., Baklaić Ž., Ljubičić M., Kolarić B., Draženović V.**: "*Influenza epidemiology in Croatia and preparations for potential pandemic*", Croatian National Institute of Public Health, September 2006

[21] Croatian Parliament: "*Act on Dangerous Goods Transportation*", Zagreb, Croatia, July 2007